

REMARKS

1. Amendments to the Claims

Claims 1, 39, 43, 44 and 87 have been amended. But these amendments are minor in nature, made to overcome rejections under § 112, second paragraph, and do not, therefore, raise any new issues after final rejection.

2. Examiner Interviews

The helpfulness and courtesies extended by the Examiner to Applicants' representatives and the co-inventor during the interview on April 23, 2008 are sincerely appreciated. A statement of the substance of the interview was filed on May 15, 2008, so those comments will not be repeated herein.

The undersigned also appreciates the Examiner's time for the telephone interview on August 19, 2008 to discuss why Applicant's Response of June 24, 2008 was not entered.

3. Advisory Action and Status of the Application

Applicants filed a response to the final Office Action on June 24, 2008. In the Advisory Action dated August 1, 2008, the Examiner indicated that Applicants' Amendment of June 24th would not be entered because it "supplies new evidence". That alleged new evidence consisted of a brief summary of relevant disclosures in Applicants' specification (Exhibit 1) and a courtesy copy of the Board of Appeals decision in *Ex parte Kubin* (Exhibit 2). In the telephone interview of August 19, 2008, Applicants' representative explained why Exhibits 1 and 2 are not "new evidence" and cannot be a valid basis for refusing consideration and entry of Applicants' Amendment of June 24, 2008. In a telephone message on August 21, 2008, the Examiner advised that her position would still be maintained.

Therefore, the present response is being filed without the two exhibits attached to Applicants' response of June 24, 2008. Thus, the basis alleged by the Examiner for refusing to enter and

consider Applicants' previous response no longer is relevant. In addition, the only claim amendments made in the present response relate to minor corrections and do not in any way raise new issues or attempt to enter new matter.

Therefore, the present response should receive full consideration and be entered into the file.

4. Objections to the Specification

The Examiner has objected to the Specification with regard to missing sequence identifiers at pages 8 and 10. Those portions of the Specification have been amended to appropriately insert required SEQ. ID. NOS.

5. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

The Examiner has objected to claims 34 and 44 as lacking proper antecedent basis. Both of the claims have been amended in a manner believed to obviate the Examiner's objections. Reconsideration and withdrawal of the rejections are requested.

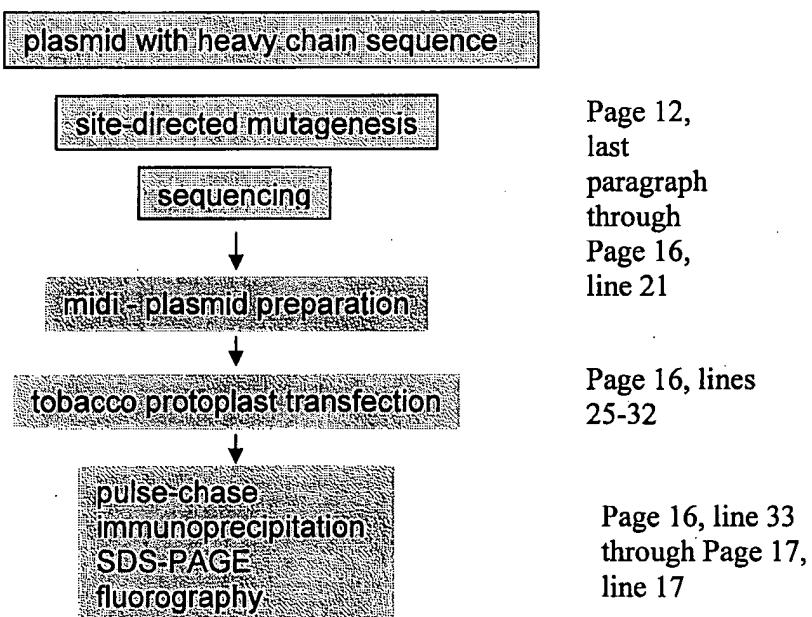
6. Claim Rejections – 35 U.S.C. § 112, First Paragraph – Written Description

Claims 1, 34-38, 40-44, 46, 48, 50, 52 and 82-87 have been rejected under 35 U.S.C § 112, first paragraph, as allegedly failing to comply with the written description requirement. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

First of all, the Examiner is reminded the written description requirement cannot be mechanistically applied. Rather, the "requirement must be applied in the context of the particular invention and the state of the knowledge." *Capon v. Eshhar*, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005). In the resent case, Applicants note that the claims under prosecution are directed to a method of making antibody molecules. All of the Examiner's comments with regard to the written description rejection relate to an alleged lack of a reasonable number of working examples of the modified nucleotide sequence. None of the Examiner's comments even address

the written description support for the method steps recited in Applicants' claims. As such, Applicants again submit that the Examiner has failed to meet her burden, with either sufficient evidence or technical reasoning, to establish that the claims do not have sufficient written description support.

Applicants submit that the Specification does indeed provide adequate written description support for the claimed method, sufficient to establish that the Applicants, in the Specification, conveyed to those of skill in the art that the Applicants were in possession of the claimed invention at the time of filing. See, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111, (Fed. Cir. 1991). Below is a summary of the basic process steps described in the present application that one skilled in the art would follow to make and use (including screening) various useful embodiments within the scope of the present claims.



Since Applicants have provided a description of the method of the invention in its full scope, Applicants clearly conveyed to those skilled in the art that they had possession of the full scope of the claimed invention at the time of filing.

Even considering the products made from Applicant's claimed method, the Specification provides adequate written description support for the current claims. Applicants in the Specification have shown that complete deletion of the C-terminal 18 amino acids of the immunoglobulin heavy chain results in reduced vacuolar targeting, and increased secretion of the assembled tetramers. (See page 22 of the Specification). Additional modified heavy chain sequences are described at pages 24-25 of the application, and are recited in claim 39.

Applicants submit that all of the evidence clearly establishes that Applicants' claims find sufficient written description support in the present application, and that the Examiner's criticisms to the contrary are improper.

In the middle of page 8 of the Office Action, the Examiner discusses the Declaration of Dr. Vitale submitted with Applicants' previous response. Before discussing the substance of the Declaration, the Examiner urges that "Dr. Vitale effectively disavows any priority claim for subject matter of instant application to the PCT filing date...and the foreign priority date". Dr. Vitale simply made no such statement and in no way disavowed any priority claim for the present application. It appears that the Examiner's comment is based simply on Dr. Vitale's statement that "one skilled in the art as of the filing date of the present application (May 18, 2005) would have been able to repeat the claimed invention across its full breadth using the teaching of the application as filed in combination with his common general knowledge". This statement merely means exactly what it says, that Dr. Vitale believes the application as filed in the United States provided an enabling disclosure across the full breadth of the claimed invention. Dr. Vitale's Declaration says nothing about any claims for priority and, therefore, should not in any way be interpreted as disclaiming any claim for priority. Applicants' claim for priority to both the PCT application and the U.K. priority application have been properly asserted and are maintained.

For all the above reasons, reconsideration and withdrawal of the written description rejection are requested.

7. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 1, 34-38, 40-44, 46, 48, 50, 52 and 82-86 have been rejected for alleged lack of enablement. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Much of the Examiner's reasoning in the enablement rejection is the same or very similar to the Examiner's reasoning in the written description rejection, so the above comments in response to the written description rejection are also relevant to rebutting the Examiner's comments with respect to the enablement rejection.

Applicants submit that the Examiner has the initial burden to provide evidence or sound scientific reasoning to object to the enablement provided by Applicants' Specification. This the Examiner has not done in the present application. As noted above, the claims under prosecution are directed to a method of making an antibody molecule. The Examiner has not even attempted to explain how one skilled in the art would not be able, with the teachings in the Specification and the knowledge in the art to:

- a) provide a nucleotide sequence encoding an immunoglobulin heavy chain;
- b) modify the nucleotide sequence within the C-terminus 18 amino acids to remove or reduce the effectiveness of vacuolar targeting;
- c) inserting the modified nucleotide sequence in the host cell; and
- d) causing the host cell to express the modified nucleotide sequence to form a modified immunoglobulin heavy chain and secret the modified immunoglobulin heavy chain from the host cell.

Applicants in their prior response responded to the Examiner's enablement rejection with the explanation in paragraph 4 of the Vitale Declaration. The Examiner has not truly addressed the

substance of those comments, or explained why the portions of the Specification referred to in the Vitale Declaration would not enable one skilled in the art to practice the full scope if the claimed invention.

Applicants submit that the reasoning of the Examiner's enablement rejection has also been rejected by the Board's decision of *Ex parte Kubit*, 83 USPQ2d 1410 (Bd. Pat. App. & Int. 2007). In *Kubit*, the Board reversed the Examiner's enablement rejection noting that "the amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art". *Id* at 1416. In the present case, as discussed above and in the Vitale Declaration, the techniques for practicing the full scope of Applicants' invention are well described in the present application, including a screening assay, such that one skilled in the art utilizing steps routine to those skilled in the art, could practice the full scope of Applicants' claimed invention.

On page 11 of the Office Action the Examiner urges that the Specification is not enabling across different species of host cells. First of all, while the Examiner raises a question, this falls far short of meeting the Examiner's burden to support any enablement rejection with suitable evidence or scientific reasoning.

In addition, as discussed above, results reported after the filing of the present application in the *Hunter et al.* publication confirm that vacuole sorting signal sequences do indeed work across species, contrary to the Examiner's assumption.

For all the above reasons, reconsideration and withdrawal of the enablement rejection are requested.

8. Prior Art Rejections

Claims 1, 34, 35, 38, 40, 41, 46, 48 and 50 have been rejected under 35 U.S.C. § 103 (a) over *Frigerio et al.* in view of *Vitale* and *Raikhel, Koide et al.* and *Matsuoka et al.* This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the Examiner's prior art rejection is merely a conclusory statement of obviousness, without properly considering whether the prior art actually teaches the individual limitations in Applicants' claims. The most glaring error in the Examiner's rejection is a failure to recognize the lack of any disclosure in the prior art with respect to step (b) in Applicants' claim 1. This step importantly recites modifying the nucleotide sequence encoding the immunoglobulin heavy chain "in the region of a nucleotide sequence encoding the C-terminus 18 amino acids". Nothing in the prior art discloses this feature of Applicants' invention, and the Examiner has not even asserted that any prior art reference teaches this aspect of Applicants' claims.

It is a fundamental principal of patent law that "all limitations of a claim must be considered in determining the claimed subject matter as is referred to in 35 U.S.C. 103 and it is error to ignore specific limitations distinguishing over the reference." *Ex parte Murphy and Burford*, 217 USPQ 479, 481 (Bd. Pat. App. & Int. 1982); citing *In re Boe*, 184 USPQ 38 (CCPA 1974). See also, *Ex parte Mohammed*, (unpublished) Appeal 2007-3395, at page 15 (Bd. Pat. App. & Int. 2007). Absent any teaching of the important limitations of Applicants' claims, the Examiner's rejection is improper under 35 U.S.C § 103, and must be withdrawn.

9. New Rejections Under 35 § 112, Second Paragraph

The Examiner has rejected claims 39, 43, 44 and 87 as being indefinite because of minor matters relating to claim format. Each of the claims has been amended in a manner believed to obviate the Examiner's rejections, so reconsideration and withdrawal of the rejections are requested.

Application No. 10/535,433
Amendment dated August 21, 2008
Reply to Office Action of January 25, 2008

Docket No.: 1009-0118PUS1

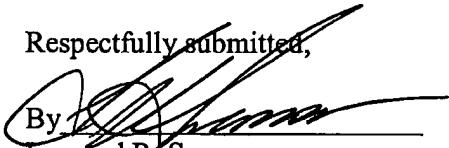
In summary, Applicants submit that the Examiner's written description, enablement and prior art rejections are not well founded for the reasons discussed above, and have been, in any event, fully rebutted. Applicants submit that, therefore, all of the rejections should be withdrawn and the claims should be allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: August 21, 2008

Respectfully submitted,

By 

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